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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MCKENZIE, THOMAS C	
ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 01/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/037,110	CALDIROLA ET AL.	
	Examiner	Art Unit	
	Thomas McKenzie, Ph.D.	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2003 and 31 October 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,22-25,27-30,32-44 and 46-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *32* is/are allowed.

6)☒ Claim(s) *1-5,11-14,18,22-25,27-30,33-40,44,46-49 and 54-60* is/are rejected.

7)☒ Claim(s) *6-10,15-17,41-43,50-53 and 61* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to amendments filed on 11/21/03. Applicants' prior amendment and remarks filed on 10/31/03 are noted. The net result of the two amendments is that Applicant has amended claims 1-3, 12-28, 28, 30, 36-43, and 47. Applicant has canceled claims 19-21, 31, and 45. Claims 48-61 are new. Claim 30 is marked as amended but the Examiner can see no changes. There are fifty-five claims pending and fifty-five under consideration. Claims 1-18, 28-30, 32-43, and 47-53 are compound claims. Claim 22, 23, 46, and 59-61 are composition claims. Claims 24, 25, 27, 44, and 54-58 are use claims. This is the third action on the merits. Claim 32 was previously allowed. Objection was previously made to claims 8, 10, 16, 17, 42, and 43. All other pending claims had been rejected. The application concerns some 1-sulfonylindole compounds, compositions, and uses thereof.

Response to Amendment

2. Applicants' deletion of piperazine as a possible substituent R^4 overcomes the art rejections made in points #9, #13, and #14 over Kelly (US 2002/0115670 A1, Ref AB). Kelly (US 2002/0115670 A1, Ref AB) teaches on piperazine radicals at position 4. This deletion of also overcomes the art rejections made in points #10 and #15 over Briggs (US 2003/0045527 A1). Briggs (US 2003/0045527 A1) also teaches only piperazine compounds.

Priority

3. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(a) as follows: the later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994). The Swedish application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 1-18, 22-30, 32-44, 46, and 47 of this application. The present claims are to molecules with 12 different heterocyclic radicals attached either to position 4, position 5, or both positions of an indole core. Swedish Application 0003810-9 discloses indole compounds with only nine different heterocyclic radicals attached to the indole core. A benzyl group is a presently claimed R_6 substituent on these heterocyclic radicals. In the Swedish parent it is not.

4. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged. However, the provisional application upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 1-18, 22-

30, 32-44, 46, and 47 of this application. The contents of this provisional application appear identical to those of Swedish Application 0003810-9 discussed above.

Applicants make two arguments concerning the support for the present claims in the priority documents. Firstly, that the teaching in the priority document that $R_4 = R_5$ means that the heterocycle radicals may be attached to either position 4 or position 5. Secondly, that the amine heterocycle radicals pictured in lines 10 and 11 page 3 of the Swedish Application are all heterocyclic compounds and therefor Applicants have support for any heterocycle, even those not pictured. The first point is persuasive but the second is not persuasive. The presently claimed radicals listed fifth, ninth, and tenth in the present definition of R_4 and R_5 in claim 1 are simply not to be found in the priority documents. Any suggestion that R_4 or R_5 can be heterocycle generally is not found in the priority documents. Addition of these three new radicals to the priority documents would constitute new matter. Applicants' change to the sixth pictured radical, the [2.2.2] azoctane corrects an obvious typo concerning hydrogen location and is not new matter.

New claims 48 and 49 have the same R_4, R_5, and R_6 radicals as listed in the priority documents. All the species of the present claim 50 are named in the

priority documents. Thus, claims 1-18, 22-30, 32-44, 46, and 47 have an effective filing date of 10/22/01. Claims 48-61 have an effective filing date of 10/20/00.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24, 25, 34, 35, and 44 remain rejected and claims 54-57 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The phrase "a disease mediated by the serotonin-related 5-HT_6 receptor" is indefinite. What are these disorders? In line 27, page 1 and in lines 20-22, page 2 Applicants list some specific diseases they intend to treat. However, these passages use open language and do not specifically identify which diseases fall into this category. The phrase "a CNS disorder" is indefinite because all this does is provide the location of the disease. Lines 20-21, page 3 list schizophrenia, Parkinson's, and depressions as CNS disorders. Are these all? Is ADHD or drug abuse such a disorder? How about brain cancer, ALS, or bipolar disorder? Determining whether a given disease responds or does not respond to such a receptor antagonist and thus, covered by the claim language, will require extensive and potentially inconclusive clinical research. With out such clinical

research to identify the patients and diseases Applicants intend to treat, the physician skilled in the clinical arts cannot determine the metes and bounds of the claim. Hence, the claims are indefinite. The Examiner suggests listing the diseases that Applicants' intend to treat in the claims being mindful of enablement requirements.

Applicants make two assertions concerning this rejection. Firstly they assert that the term is art-recognized. Secondly, they assert that any single mention, anywhere, and at any time that a specific disease is related to the 5-HT_6 receptor means that the phrase is forever linked to the disease. This is not persuasive. Assertion is not evidence and the fact the literature is contradictory as to the diseases included surely must mean that no art-recognized list of such diseases exits. Secondly, if a disease, once listed, is later found to be not associated with the 5-HT_6 receptor, then surely that is an error that has been corrected in the literature. The art-recognized status of the linkage would then disappear as soon as the error is corrected. For example Lindner (JPET) teaches that there was a hypothesis that 5-HT6 Receptor Antagonists were thought enhance cognition in animal models of learning and potentially be useful for Alzheimer's treatment. The conclusion reached after complex experimentation was, "our experiments are not consistent with previous reports that suggested that 5-HT6 antagonists might have

therapeutic potential for cognitive disorders." How can cognitive disorders remain "a disease mediated by the serotonin-related 5-HT_6 receptor" after September 15, 2003 in view of such evidence? Lindner (JPET) also demonstrates the complex experimentation required to establish the metes and bounds of Applicants' claims.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24, 25, 27, and 44 remain rejected and claims 54-58 are newly rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating depression and psychosis, does not reasonably provide enablement for treating obesity, every "CNS disorder", or every "disease mediated by the serotonin-related 5-HT_6 receptor". The specification does not enable any physician skilled in the art of medicine, to use the invention commensurate in scope with these claims. "The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. a) Determining if any particular claimed

compound would treat every CNS disease or every "disease mediated by the serotonin-related 5-HT_6 receptor" would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it clinical trials with a number of fundamentally different diseases which occur in the brain and spinal column, a large degree of experimentation. b) The direction concerning treating such diseases is found in the lines 20-22 on page 2, which merely states Applicants' intention to do so. Applicants describe formulations in the passage spanning line 11, page 10 to line 17, page 11. Applicants describe doses in lines 18-26, page 11 and propose a 50,000-fold range of doses. Since, as discussed below, no pure "serotonin-related 5-HT_6 receptor" agent has ever been used to treat any human disease, how is the skilled physician to know what dose to use? Applicants provide no dosing schedules required to practice their invention. There is a single *in vitro* binding assay described in lines 1-20, page 61 with no data. It is unclear if this assay is related to all CNS diseases. It is also unclear if the Applicants' compounds are agonists or antagonists at "the serotonin-related 5-HT_6 receptor". Without understanding if a compound is an agonist or an antagonist, there is no way for a physician to know how to use a compound. There is a single obesity related disease model in the mouse described in the passage spanning line 21, page 61 to line 10, page 63. Again there is no data presented. c) There is no working

example of treatment of any disease in man or animals. d) The nature of the invention is clinical treatment of disease, which involves physiological activity. e) The state of the clinical arts in "disease mediated by the serotonin-related 5-HT_6 receptor" is found in the review of Robichaud (Ann. Reports Med. Chem.). He reports in the final sentence on page 16 that several nonselective agents bind to this receptor. The final part of the preceding sentence makes clear that in 2000, experimental work was under way to determine if selective binding agents were useful therapeutically but as of that date none were understood to be so.

f) The artisan using Applicants invention would be a physician with a MD degree, board certified in psychiatry and several years of experience. g) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

h) The scope of the claims involves all of the hundreds of thousands of compounds of claim 1 as well as the hundred of diseases embraced by the term CNS disease. These include manic depression, neurological disturbances, ALS, Alzheimer's disease, Huntington's disease, spinal cord injury, sexual disorders, stroke, and pain all of which are included in the term CNS disorders. MPEP

2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to practice Applicants' therapeutic claims.

Applicants make three arguments concerning this rejection. Firstly, they assert that the artisans who would practice Applicants claims would be researchers at a pharmaceutical company and that the experimentation described above, albeit complex, is routine in the pharmaceutical industry. Secondly, that the two assays discussed above are correlated to all such treatments. Thirdly, that Robichaud (Ann. Reports Med. Chem.) does not represent the state of the art and that compounds binding to other serotonin receptors in addition to binding to the 5-HT_6 receptor are useful therapeutic agents.

This is not persuasive. The claims are not drawn to searching for new drugs; rather they are drawn to treating illnesses. Only a physician can practice treatment in humans. The direction in the specification must be directed to the physician who will actually treat the claimed diseases. Independent of who the practitioner

will be, Applicants is referred to *University of Rochester v. G. D. Searle & Co.,* 68 USPQ2d 1424 at 1438, where Judge Larimer held that screening 600 compounds by two drug company employees was a non-routine matter. What would Judge Larimer think of Applicants' plan to synthesize and screen hundreds of thousands of compounds?

Secondly, assertion of correlation is not evidence of such a correlation. Where are the journal articles or experimental data demonstrating that most compounds that are active in Applicants' binding assay are efficacious for the entire scope of every CNS disease? Applicants do not assert in the specification and it is not art-recognized that the two assays described are correlated to clinical efficacy for treatment of any disease, let alone all CNS diseases. In the absence of any data what so ever for their compounds, what do Applicants intend to correlate? Which 1 of Applicants' 100,000 compounds was tested in the obese mouse assay? Since the present tense is used, is this a prophetic example? Assuming that one compound had been tested, how does that provide enablement for the full scope of the 100,000 compounds whose use is claimed? Applicants are reminded of the requirement in *Ex parte LANHAM* 135 USPQ 106, "[i]t is our opinion that the statutory requirement of a disclosure of utility must be found in the specification as originally filed and cannot be supplied by way of argument or affidavit. If

appellant, in fact, knew of this particular utility for the product of his process, it should have been disclosed in the specification."

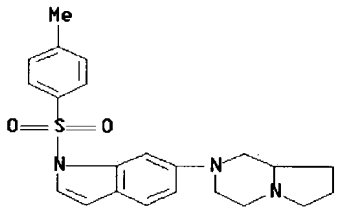
While Robichaud (Ann. Reports Med. Chem.) does discuss the therapeutic utility of compounds binding to other serotonin receptors in addition to the 5-HT_6 of the present application. Since Applicants do not assert and provide no evidence that their compounds bind to any other receptor type, the efficacy of such broadly active agents has no bearing upon the present claims. Where is the evidence that compounds witch bind to the 5-HT_6 receptor and which are not separated as to agonist or antagonist are able to treat every CNS disease, brain cancer and Alzheimer's disease included? Dourish (Obes Res.) says in his abstract that the 5-HT_6 receptor "remains unexplored" and that "development of selective ligands for th[is] site has the potential to lead to new treatments for obesity" Potential is not the standard for enablemnt. Substantiation of use and scope is required when the use is "speculative", "sufficiently unusual", or not provided in the specification, *Ex parte Jovanovics,* 211 USPQ 907, *In re Langer,* 183 USPQ 288, *Hoffman v. Klaus*, 9 USPQ2d 1657, and *Ex parte Powers*, 200 USPQ 925 concerning the type of testing needed to support *in vivo* use claims. Also see the MPEP § 2164.03 for enablement requirements in the structure sensitive arts of pharmacology and medicinal chemistry.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 11-13, 14, 22, 24, 27-30, 33-40, 44, 46, and 47 remain rejected and claims 18, 23, 48, 49, 54, 55, 57, 59, and 60 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over Isaac (Bioorganic & Medicinal Chemistry Letters, ref ADD). The reference teaches the compound with registry number 299433-11-7 shown below. The Applicants claim the compounds with the



hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl radical attached at either position 4 or position 5 of the indole core. The reference teaches a compound with hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl radical attached at position 6 of the indole core. The compound shown in the reference in Figure 1, page 1720 and is compound **4b**. A second relevant compound is **4a**. The difference between the claimed and taught compounds is the point of attachment of the heterocyclic

radical. Applicants claim attachment at positions 4 or 5 and the reference teaches attachment at position 6. These are *per se* obvious ring position isomers and require no specific teaching.

Isaac (Bioorganic & Medicinal Chemistry Letters, ref ADD) appeared in the 15 issue of Volume 10. A photocopy of the cover page of this issue is provided for Applicants convenience. Issue No. 15 has a publication date of 7 August 2000 and, in fact, was received by the USPTO library on Aug 1, 2000.

In the last sentence, first paragraph, second column, page 1720 Isaac (Bioorganic & Medicinal Chemistry Letters, ref ADD) teaches that "specific concentrations of test compounds" were prepared. These presumably were in water, saline , or buffer and are compositions. Thus, Applicants claims 22 and 46 are made obvious. Binding data for the 5-HT_6 receptor are presented in Table 1, page 1720. Selectivity for the 5-HT_6 receptor for compound **4a** is presented in Table 2, page 1720. The expectation that compound **4a** is useful for treating schizophrenia, depression, and memory dysfunction is taught in the final paragraph on page 1721. Thus, Applicants' claims 24, 27, 44, and 46 are made obvious.

The synthesis taught by Isaac (Bioorganic & Medicinal Chemistry Letters, ref ADD) is a coupling reaction, similar to that used by Applicants. Synthesis of the ring position isomers of the compounds of this reference requires only use of a

ring position isomeric bromo-indole. Thus, the reference is an enabling disclosure for the synthesis of Applicants' claimed compounds.

Applicants' claim 18 did not previously list the indolizidinyl species but now it does. Nowhere is this addition indicated. The 5-aza-indolizinyl radical is Applicants' name for the hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl radical pictured above.

Applicants argue that there is no teaching within the reference to move the point of attachment, that the reference is not enabling for making Applicants' compounds, and finally offer exhibit A concerning water solubility properties of position-6 isomers contrasted to position-4 isomers.

This is not persuasive. Concerning the first argument, these are per se obvious ring position isomers and no secondary teaching is required. It would be routine for the medicinal chemist to vary the point of attachment in order to increase potency and to establish better patent protection for her compounds.

Concerning the second argument, while a bromine atom at the six position of an indole, ring, as in the intermediate used by Isaac (Bioorganic & Medicinal Chemistry Letters, ref ADD) is *meta* to the indole nitrogen, it is *para* to the methine carbon atom of the five- membered ring. The 4-bromo compound required to make one set of Applicants compounds would have the bromine atom

meta to the indole nitrogen and ortho to the methine carbon atom of the five-membered ring. It is unclear why Applicants expect this subtle electronic difference to effect reactivity. In any case the reaction used by both the reference and Applicants is a palladium metal catalyzed coupling reaction, not an electrophilic substitution reaction. Thus, it is not sensitive to the electronic effects postulated by Applicants.

Concerning the third argument, Exhibit A is not persuasive as demonstrative of unexpected results. Firstly, it is not a proper Rule 132 declaration. Secondly, the utility of Applicants compounds is the treatment of depression and psychosis. Applicants' demonstration of that utility is shown by *in vitro* binding assay. Water solubility of a compound is only weakly linked to its ability to treat depression and psychosis. Water solubility was not a test used by Applicants in their search for active compounds. If a claimed compound has both a close structural and biological property in common with a known compound, then some unexpected secondary property does not make the claimed compound patentable, *Imperial Chemical Industries, PLC, et al. v. Mossinghoff, Commissioner of Patents and Trademarks*, 223 USPQ 769 (a steroid having an ethyl group in place of the chlorine atom or the hydrocarbon group of the prior art and having the same anti-

estrogen activity as the prior art but having less severe side effects in the treatment of breast cancer was still obvious.)

Thirdly, the compound of the prior art has a naphthalene group at position 1 and a hexahydropyrrolo[1,2-a]pyrazin-2(1H)-yl radical at position 6. Applicants' allegedly superior compounds have a phenyl group at position 1 and a piperazine group at position 4 and a 2,5-dimethoxyphenyl group at position 1 and a piperazine at position 4 respectively. In submitting evidence of unobvious results the examples must represent the closest prior art. See *Ex parte Gelles* 22 USPQ2d 1318, *In re Borkowski*, 184 USPQ 29, *In re Goodman*, 339 F.2d 228, 144 USPQ 30. The closest prior art have neither a piperazine at position 6 nor phenyl or 2,5-dimethoxyphenyl group at position 1 as do the examples used by Applicants.

Finally, the lower water solubility is not unexpected. Applicants' compounds have a piperazine with an NH group at position 4. The prior art compound has a radical with three additional carbon atoms and no NH group. Both factors will make Applicants compounds more soluble. The prior art compound has naphthalene, with 10 carbon atoms, at position 1. Applicants' compounds have a phenyl with six carbon atoms or 2,5-dimethoxyphenyl group, with eight carbon atoms and two oxygen atoms at position 1. Decreasing the size of Applicants molecules will naturally increase the water solubility. For example,

0.03g of naphthalene will dissolve in a liter of water but 0.82g of benzene will dissolve in the same amount of water. This is a twenty-seven-fold increase for this one factor alone. Thus, the changes in solubility shown by Applicants cannot be ascribed only to changes in location of substitution on the indole ring.

Allowable Subject Matter

8. Claim 32 remains allowed. Claims 6-10, 15-17, 41-43, 50-53, and 61 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

9. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

10. Please direct any inquiry concerning this communication or earlier communications from the Examiner to Thomas C McKenzie, Ph. D. whose telephone number is (703) 308-9806. After February 9, 2004, the Examiner may be reached at (571) 272-0670. The FAX number for amendments is (703) 872-9306. The PTO presently encourages all applicants to communicate by FAX. The Examiner is available from 8:30 to 5:30, Monday through Friday. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mukund Shah can be reached on (703) 308-4716. Please direct general inquiries or any inquiry relating to the status of this application to the receptionist whose telephone number is (703) 308-1235.

Mukund Shah
Supervisory Patent Examiner
Art Unit 1624

TCMcK